REMARKS

Claims 1-10, 12, and 18-22 are pending in this application. Claims 1-10, 12, and 18-22 stand rejected. Claims 2, 4-5, and 7 stand objected to. The Applicants herein cancel Claims 3, 7, 10-17, 20-22 without prejudice or disclaimer to the subject matter contained therein. Claims 1, 2, 4-6, 8, 9, and 19 have been amended. By amendment herein, the applicants add new Claim 23. Support for these new and amended claims can be found in the as-filed claims and specification. Accordingly, these amendments introduce no new matter. After the amendments made herein, Claims 1-2, 4-6, 8-9, 18-19, and 23 are pending in the instant application.

In view of the following amendment and response, the Applicants believe the claims presented herein are allowable. Reconsideration is respectfully requested.

OBJECTIONS TO THE CLAIMS

Claims 2, 4-5, and 7 stand objected to because "A" should have been "The" for these dependent claims. In response, the Applicants herein amend Claims 2, and 4-5 to replace "An" with "The". In addition, the applicants herein cancel Claim 7.

Claim 7 stands further objected to, because the specification allegedly fails to provide antecedent basis for "the framework of the light chain included the amino acid residues from the murine antibody at position 64 by the Kabat numbering system." The Applicants herein cancel Claim 7, therefore rendering this rejection moot. Also, none of the amended claims contain this language. Accordingly, the Applicants respectfully request reconsideration and withdrawal of the objections to Claims 2, and 4-5, and 7

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-10, 12, and 18-22 have been rejected under 35 U.S.C. § 112, first paragraph for allegedly not being enabled by the instant specification. On pages 2-3 of the Office Action, the Examiner opines that only the following nine embodiments of the invention that he states are enabled by the instant specification:

> (1) A monoclonal antibody that binds specifically to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells comprising the light chain variable domains CDRL1, CDRL2, CDRL3, heavy chain variable domains CDRH1, CDRH2, and CDRH3 wherein CDRL1 consisting of the amino acid sequence RSSKSLLY KDGKTYLN of SEQ ID NO:1, CDRL2 consisting of the amino acid sequence LMSTRAS of SEQ ID NO:5, CDRL3 consisting of the amino acid sequence QQLVEYPFT of SEQ ID NO:7, CDRH1 consisting of the amino acid sequence GYWMS of SEQ ID NO:9, CDRH2 consisting of the amino acid sequence EIRLKSDNYATHYAESVKG of SEQ ID NO:11, [and] CDRH3 consisting of the amino acid sequence FID of SEQ ID NO:13 for diagnostic purpose[.]

The applicants herein amend Claim 1 to track the Examiner's suggested language.

"(2) [T]he monoclonal antibody mentioned above which binds to CD23 with an affinity constant equal to or greater than $1x10^9$ Ka Mol^{-1}." The Applicants herein amend Claim 1 (and dependent Claim 2) accordingly.

(3) A monoclonal antibody as mentioned in (1), wherein the antibody is chimeric or humanized. The Applicants herein amend Claim 1 (and dependent Claims 4 and 5) to track the Examiner's suggested language.

"(4) The humanized antibody wherein the framework of the heavy chain retains the mouse heavy chain residues at position 49, 66, 76, 77 and 94 according to the Kabat numbering system and the framework of the light chain retains the mouse light chain amino acid residue at position 64 according to the Kabat numbering system[.]" The Applicants herein amend Claim 6, per this suggestion of the Examiner, in conjunction with his below suggestion for this claim with respect to Section 112, second paragraph, to recite: "The

monoclonal antibody according to claim 1, wherein the framework of the heavy chain retains the mouse heavy chain amino acid residues positions 49, 66, 76, 77 and 94 according to Figure 1, and the framework of the light chain retains the mouse light chain amino acid residue at position 64 according to Figure 1[.]"

"(5) An antibody which binds to the CD23 (FCRII) type II molecule expressed on haematopoietic cells comprising the amino acid sequences encoded by the nucleic acid sequences according to SEQ ID NO:1 *and* SEQ ID NO:2[.]" The Applicants herein amend Claim 8 to track the Examiner's recommended language.

"(6) An antibody which binds to the CD23 (FCRII) type II molecule expressed on haematopoietic cells comprising the amino acid sequences encoded by the nucleic acid sequences according to SEQ ID NO:17 *and* SEQ ID NO:8[.]" The Applicants herein amend Claim 9 to track this language, except that the Applicants believe that the claim should read "SEQ ID NO:17 and SEQ ID NO:18", rather than "SEQ ID NO:17 and SEQ ID NO:8".

"(7) A pharmaceutical formulation comprising the antibody as set forth in claim 1 and a pharmaceutically acceptable excipient." The Applicants herein amend Claim 18 accordingly.

"(8) A pharmaceutical formulation comprising the antibody as set forth in claim 1 in combination with an anti-inflammatory agent and a pharmaceutically acceptable excipient." The Applicants herein add Claim 19, which claims this embodiment.

"(9) A method of making any antibody mentioned above for diagnostic purpose and for screening for antibody which competitively inhibits the binding of any antibody mentioned above[.]" The Applicants herein cancel Claim 20.

"(10)" A method of treating rheumatoid arthritis comprising administering the specific antibody mentioned above[.]" The Applicants herein add new Claim 23, which

recites: "A method of treatment of rheumatoid arthritis in a patient in need thereof, said method comprising the step of administering to the patient a pharmaceutically effective amount of the monoclonal antibody according to claim 1."

On pages 3-5 of the Office Action, the Examiner lists the embodiments that he considers not to be enabled by the instant specification. That the Applicants herein amend all of the pending claims to cover the above embodiments that the Examiner admits are enabled by the specification overcomes all of these rejections. Moreover, the instantly pending claims, as amended, do not recite the embodiments that the Examiner considers non-enabled. Claim 1, and the dependent claims, all recite the specific monoclonal antibody that the Applicants made that binds to CD23 (FCεRII). For this reason, the Applicants submit that the instant specification teaches the skilled artisan how to make and use the instantly claimed invention without undue experimentation.

On pages 6 and 7 of the Office Action, the Examiner alleges that the specification fails to teach the skilled artisan how to use the claimed CD23 monoclonal antibody to treat the following list of diseases recited in Claim 12: lupus, erythematosus, Hashimotos thyroiditis, multiple sclerosis, uveitis, dermatitis, psoriasis, urticaria, nephritic syndrome, glomerulonephritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, Sjogren's syndrome, rhinitis, eczema, GVH, CPIA, insulitis, bronchitis (particularly chronic bronchitis), diabetes (particularly Type I diabetes), and B-cell malignancies. The Applicants herein cancel Claim 12, rendering this ground of rejection moot. The only remaining claimed method of treatment is new Claim 23, which covers a method of treatment of rheumatoid arthritis with the monoclonal antibody that binds to CD23 (FCεRII). As mentioned above, the Examiner admits in point (9) quoted above, that the instant specification enables this method of treatment.

The Examiner further argues, at the paragraph bridging pages 7 and 8, that the instant specification does not teach how to make any antibody which competitively inhibits the binding of antibody having the CDR sequence set out in Claim 1 to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells, the subject matter of Claims 3, 21, and 22. As the Applicants herein cancel Claims 3, 21, and 22, this ground of rejection is now moot.

The Examiner also argues that the instant specification fails to enable Claims 8 and 9. Specifically, he contends that the specification provides "insufficient guidance as to the structure of the other amino acid sequence encoded by the other polynucleotide sequence in the claimed antibody which binds to the CD23 (FCεRII) type II molecule that is expressed on haematopoietic cells. As amended herein, Claim 8 recites: "A diagnostic antibody that binds to the CD23 (FCRεII) type II molecule expressed on haematopoietic cells comprising both of the amino acid sequences encoded by the nucleotide sequences according to SEQ ID NO:1 and SEQ ID NO:2." Moreover, as amended herein, Claim 9 recites: "A diagnostic antibody that binds to the CD23 (FCRεII) type II molecule expressed on haematopoietic cells comprising both of the amino acid sequences encoded by the nucleotide sequences according to SEQ ID NO:17 and SEQ ID NO:18." The Applicants submit that Claims 8 and 9, as amended, contain sufficient guidance as to the structure of the other amino acid sequence encoded by the other polynucleotide sequence in the disclosed CD23 antibody.

Claims 1-10, 12, and 18-22 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner argues that the specification does not reasonably provide a written description of the embodiments of the

invention that comprise the subject matter of these claims. The Applicants herein cancel Claims 3, 7, 10, 12, and 20-22.

On the paragraph bridging pages 13 and 14, the Examiner lists the following embodiments for which he admits that the instant specification provides sufficient written description:

(1) A monoclonal antibody that binds to CD23(FCεRII), a type II molecule expressed on haematopoietic cells wherein the antibody comprises the amino acid sequences encoded by the nucleotide sequences encoded by the nucleotide sequences according to SEQ ID NO:1 *and* SEQ ID NO:2 for detection of disorders such as the ones recited in Claim 12. The Applicants herein amend Claim 8 to track this suggested language.

(2) A humanized antibody that binds to CD23(FCεRII), a type II molecule expressed on haematopoietic cells comprising the amino acid sequences encoded by the nucleotide sequences according to SEQ ID NO:17 *and* SEQ ID NO:18. The Applicants herein amend Claim 9 to mimic this suggested language.

(3) The monoclonal CD23 antibody that binds to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells comprising light chain variable domains CDRL1, CDRL2, CDRL3, heavy chain variable domains CDRH1, CDRH2, and CDRH3 wherein CDRL1 consists of the amino acid sequence RSSKSLLY KDGKTYLN of SEQ ID NO:1, CDRL2 consists of the amino acid sequence LMSTRAS of SEQ ID NO:5, CDRL3 consists of the amino acid sequence QQLVEYPFT of SEQ ID NO:7, CDRH1 consists of the amino acid sequence GYWMS of SEQ ID NO:9, CDRH2 consists of amino acid sequence EIRLKSDNYATHYAESVKG of SEQ ID NO:11, and CDHR3 consists of amino acid sequence FID of SEQ ID NO:13. The Applicants herein amend Claim 1 to track this suggested language. The Examiner states further that the instant specification further

discloses the affinity constant (Ka) for this monoclonal antibody, which the Applicants recite in Claim 2, as amended.

The Examiner further argues that there is inadequate written description about the amino acid residues at the cited positions from which murine antibody to be included in the framework of the heavy chain (Claim 6) and the light chain (Claim 7). The Applicants herein cancel Claim 7, and incorporate the limitations of Claim 7 into Claim 6, as amended. Claim 6, as amended, now recites an antibody that contains both the heavy and light chain variable regions of the disclosed monoclonal antibody, and ties the specific amino acid residues of these heavy and light chain variable regions to Figures 1 and 2, respectively.

The Examiner also contends that there is inadequate written description about the framework of the heavy and light chain in Claims 1-2 because SEQ ID NOs:3, 5, 7, 9, 11, and 13 are merely fragments of the variable regions of a monoclonal antibody. Claim 1, as amended, now recites the specific structure of both the heavy and light chain variable regions, giving the amino acid sequence for each of the 6 CDRs.

The Examiner further argues that Claims 8 and 9 lack adequate written description about the other amino acid sequences encoded by the other nucleotide sequences because the term, "or", merely requires one or the other sequence. The Applicants herein amend Claims 8 and 9 to require both of the recited sequences, thus adequately describing the claimed antibody. Because the structure of the monoclonal antibody of Claim 1 is now adequately described, the Applicants submit that pharmaceutical compositions comprising this antibody, the, subject matter of Claims 18 and 19, as amended, is also adequately described.

They also herein amend Claims 1, 2, 4-6, 8, 9, and 19 to recite the specific, disclosed monoclonal antibody that binds to CD23 (FCεRII) type II molecule that is expressed on haematopietic cells.

The Applicants respectfully submit that, in view of the forgoing remarks and the claims as amended, the Applicants have overcome the rejection of Claims 1-10, 12, and 18-22 under 35 U.S.C. § 112, first paragraph. Accordingly, the Applicants respectfully request withdrawal of these rejections.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 6-7 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. First, the Examiner opines that the recitation of "the framework of the heavy chain *includes* the amino acid sequence residues" in Claim 6 is indefinite and ambiguous because the specific amino acid residues at position 49, 66, 76, 77, and 94 are not recited in the claim. Alternatively, the Examiner suggests that Claim 6 be amended to recite: "The antibody according to claim 1 wherein the framework of the heavy chain retains the mouse heavy chain residues at position 49, 66, 76, 77 and 94 according to Figure 1."

Likewise, the Examiner contends that the recitation in Claim 7, the "amino acid residues from the murine antibody at position 64," is ambiguous and indefinite, because the specific amino acid residue from the framework of the light chain,of which murine antibody is not recited in the claim. He suggests that the Applicants amend Claim 7 to recite: "The antibody according to claim 1 wherein the framework of the light chain retains the mouse light chain amino acid residue at position 64 according to Figure 2."

In response to these rejections, the Applicants herein cancel Claim 7, and amend Claim 6 as follows:

> The monoclonal antibody according to claim 1, wherein the framework of the heavy chain retains the mouse heavy chain amino acid residues positions 49, 66, 76, 77 and 94 according to Figure 1, and the framework of the light chain

retains the mouse light chain amino acid residue at position 64 according to Figure 2.

Claim 6, as amended, incorporates both the limitations of cancelled Claim 7, as well as the Examiner's suggested language. Therefore, the Applicant submit that Claim 6, as amended, The Applicants respectfully submit that, in view of the forgoing remarks and amendments, they have overcome the Examiner's rejection of Claim 6 under 35 U.S.C. § 112, second paragraph. Accordingly, the Applicants respectfully request reconsideration and withdrawal of this rejection.

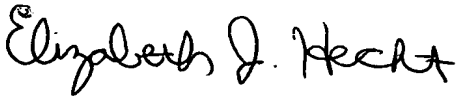
CLAIM REJECTIONS UNDER 35 U.S.C. § 102(b)

Claims 3, 21, and 22 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Waikai, *et al.* (*Hybridoma* 12(1): 25-43 (1993)) (hereinafter referred to as "Waikai"). By amendment herein, the Applicants have cancelled Claims 3, 21, and 22, thus rendering these rejections moot. Accordingly, they request withdrawal of the rejection of Claims 3, 21, and 22 under 35 U.S.C. § 102(b).

The Applicants reserve the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the cancelled claims, the claims as originally filed, and any other claims supported by the specification. The Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is

earnestly solicited. If it would expedite the prosecution of this application, the Examiner is invited to confer with the Applicants' undersigned attorney.

Respectfully submitted,



Elizabeth J. Hecht
Attorney for Applicants
Registration No. 41,824

GlaxoSmithKline
Corporate Intellectual Property - UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939
Phone (610) 270-5009
Facsimile (610) 270-5090
N:\EJH\APPLNS\PG3433\ROA1.doc